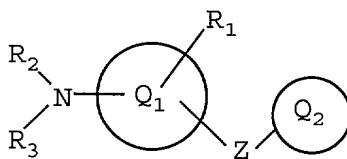


We claim:

1. A compound of formula I



I

- 5 including diastereomers, enantiomers and salts thereof

where

Q₁ is thiazolyl;

Q₂ is aryl or heteroaryl optionally independently substituted with one or more substituents R_{1a};

- 10 Z is

- (1) -O-,
- (2) -S-,
- (3) -NR₄-,
- (4) -CR₄R₅-,
- 15 (5) -CR₄R₅-O-CR_{4a}R_{5a}-,
- (6) -CR₄R₅-NR_{4b}-CR_{4a}R_{5a}-,
- (7) -CR₄R₅-S-CR_{4a}R_{5a}-,
- (8) -CR₄R₅-O-,
- (9) -O-CR₄R₅-,
- 20 (10) -CR₄R₅-NR_{4b}-,
- (11) -NR_{4b}-CR₄R₅-,
- (12) -CR₄R₅-S-,
- (13) -S-CR₄R₅-,
- (14) -S(O)_q- where q is 1 or 2,
- 25 (15) -CR₄R₅-S(O)_q-, or
- (16) -S(O)_q-CR₄R₅-;

R₁ and R_{1a} are independently

- (1) hydrogen or R₆,
- (2) OH or -OR₆,

- (3) $-\text{SH}$ or $-\text{SR}_6$,
 (4) $-\text{C}(\text{O})_q\text{H}$, $-\text{C}(\text{O})_q\text{R}_6$, or $-\text{O}-\text{C}(\text{O})_q\text{R}_6$,
 (5) $-\text{SO}_3\text{H}$ or $-\text{S}(\text{O})_q\text{R}_6$,
 (6) halo,
 5 (7) cyano,
 (8) nitro,
 (9) $-\text{Z}_4-\text{NR}_7\text{R}_8$,
 (10) $-\text{Z}_4-\text{N}(\text{R}_9)-\text{Z}_5-\text{NR}_{10}\text{R}_{11}$,
 (11) $-\text{Z}_4-\text{N}(\text{R}_{12})-\text{Z}_5-\text{R}_6$, or
 10 (12) $-\text{P}(\text{O})(\text{OR}_6)_2$;

R_2 and R_3 are each independently H, $-\text{Z}_4-\text{R}_{6a}$, or $-\text{Z}_4-\text{NR}_{7a}\text{R}_{8a}$

R_4 , R_{4a} , R_{4b} , R_5 and R_{5a} are each independently hydrogen, alkyl, aryl, aralkyl, cycloalkyl, or heteroarylalkyl;

R_6 , R_{6a} , R_{6b} and R_{6c} are independently alkyl, alkenyl, alkynyl, cycloalkyl,

- 15 cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 ,

R_7 , R_{7a} , R_8 , R_{8a} , R_9 , R_{10} , R_{11} and R_{12}

- 20 (1) are each independently hydrogen, or $-\text{Z}_4\text{R}_{6b}$; or
 (2) R_7 and R_8 , or R_{7a} and R_{8a} may together be alkylene, alkenylene, or heteroalkylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 , or
 25 (3) any two of R_9 , R_{10} and R_{11} may together be alkylene, alkenylene or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

Z_1 , Z_2 and Z_3 are each independently

- 30 (1) hydrogen or Z_6 ,
 (2) $-\text{OH}$ or $-\text{OZ}_6$,
 (3) $-\text{SH}$ or $-\text{SZ}_6$,

- 5
- (4) $-\text{C}(\text{O})_q\text{H}$, $-\text{C}(\text{O})_q\text{Z}_6$, or $-\text{O}-\text{C}(\text{O})_q\text{Z}_6$,
 - (5) $-\text{SO}_3\text{H}$, $-\text{S}(\text{O})_q\text{Z}_6$, or $\text{S}(\text{O})_q\text{N}(\text{Z}_9)\text{Z}_6$,
 - (6) halo,
 - (7) cyano,
 - (8) nitro,
 - (9) $-\text{Z}_4-\text{NZ}_7\text{Z}_8$,
 - (10) $-\text{Z}_4-\text{N}(\text{Z}_9)-\text{Z}_5-\text{NZ}_7\text{Z}_8$,
 - (11) $-\text{Z}_4-\text{N}(\text{Z}_{10})-\text{Z}_5-\text{Z}_6$,
 - (12) $-\text{Z}_4-\text{N}(\text{Z}_{10})-\text{Z}_5-\text{H}$,

10

 - (13) oxo,
 - (14) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be
alkylene or alkenylene completing a 3- to 8-membered saturated or
unsaturated ring together with the atoms to which they are attached; or
 - (15) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be
15 $-\text{O}-(\text{CH}_2)_q-\text{O}-$;

Z_4 and Z_5 are each independently

- 20
- (1) a single bond,
 - (2) $-\text{Z}_{11}-\text{S}(\text{O})_q-\text{Z}_{12}-$,
 - (3) $-\text{Z}_{11}-\text{C}(\text{O})-\text{Z}_{12}-$,
 - (4) $-\text{Z}_{11}-\text{C}(\text{S})-\text{Z}_{12}-$,
 - (5) $-\text{Z}_{11}-\text{O}-\text{Z}_{12}-$,
 - (6) $-\text{Z}_{11}-\text{S}-\text{Z}_{12}-$,
 - (7) $-\text{Z}_{11}-\text{O}-\text{C}(\text{O})-\text{Z}_{12}-$,

25

 - (8) $-\text{Z}_{11}-\text{C}(\text{O})-\text{O}-\text{Z}_{12}-$; or
 - (9) alkyl

Z_6 and Z_{6a} are independently

- 30
- (i) alkyl, hydroxyalkyl, alkoxyalkyl, alkenyl, alkynyl, cycloalkyl,
cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl,
alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl;
 - (ii) a group (i) which is itself substituted by one or more of the same or
different groups (i); or

- (iii) a group (i) or (ii) which is independently substituted by one or more of the groups (2) to (15) of the definition of Z_1 ;

Z_7 , Z_8 , Z_9 and Z_{10}

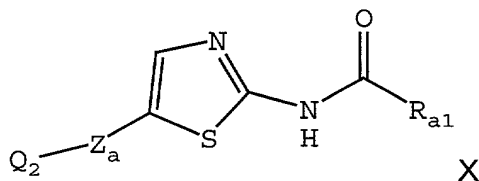
- (1) are each independently hydrogen or $-Z_4-Z_{6a}$;
- 5 (2) Z_7 and Z_8 may together be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 , or
- 10 (3) Z_7 or Z_8 , together with Z_9 , may be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

Z_{11} and Z_{12} are each independently

- (1) a single bond,
- 15 (2) alkylene,
- (3) alkenylene, or
- (4) alkynylene;

provided that said compound is other than

- (a) a compound of formula X



where

Z_a is $-\text{CR}_4\text{R}_5-$, $-\text{NR}_4-$, or $-\text{NR}_4-\text{CR}_4\text{R}_5-$;

Q_2 is as defined above;

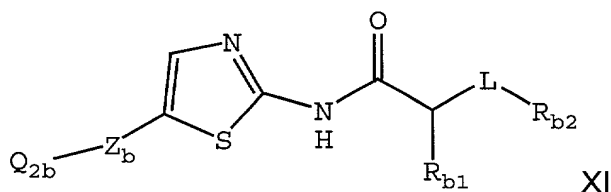
R_{a1} is alkyl, alkenyl, cycloalkyl, heterocyclo, aryl, aralkyl or $-\text{NR}_{7a1}\text{R}_{8a1}$;

- 25 R_{7a1} is alkyl, cycloalkyl, heterocyclo, aryl, $-\text{C}(\text{O})\text{aryl}$, or aralkyl; and

R_{8a1} is H, alkyl, alkenyl or alkynyl;

or R_{7a1} and R_{8a1} combine to form a heterocyclo group;

- (b) a compound of formula XI



where

Z_b is -CR₄R₅-, -NR₄-, or -NR₄-CR₄R₅-;

Q_{2b} is aryl

5 R_{b1} is H, alkyl optionally substituted with hydroxy, alkoxy, amino, alkylamino or dialkylamino;

L is phenyl or heteroaryl;

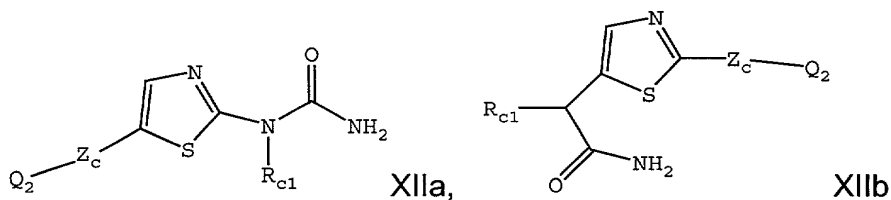
R_{b2} is -NR_{b3}R_{b4}, or -N(H)C(O)R_{b5};

R_{b3} and R_{b4} are each independently H, cycloalkyl, alkyl or aryl;

10 or R_{b3} and R_{b4} together with the nitrogen atom to which they are attached combine to form 4-morpholinyl, 1-piperazinyl, N-alkyl-piperazinyl, N-aryl-piperazinyl, N-arylalkyl-piperazinyl, piperidinyl, pyrrolidinyl, 2-oxo-1-pyrrolidinyl, imidazolyl, or 3-azabicyclo[3.2.2]nonyl; and

15 R_{b5} is carboxy, alkyl, perfluoroalkyl, alkynyl, aryl, 2-oxo-pyrrolidinyl or piperidinyl;

(c) a compound of formula XIIa or XIIb



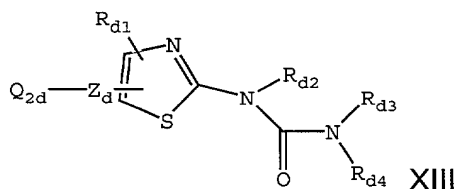
where

Q₂ is as defined above;

20 Z_c is CH₂; and

R_{c1} is aryl or heterocyclo;

(d) a compound of formula XIII



where

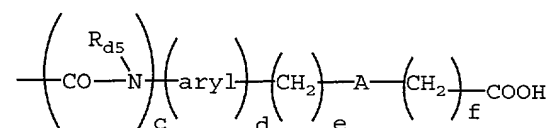
Z_d is CH_2 ;

Q_{2d} is aryl;

R_{d1} is

5 (1) $-\text{C}(\text{O})\text{NR}_{d7}\text{R}_{d8}$,

(2)



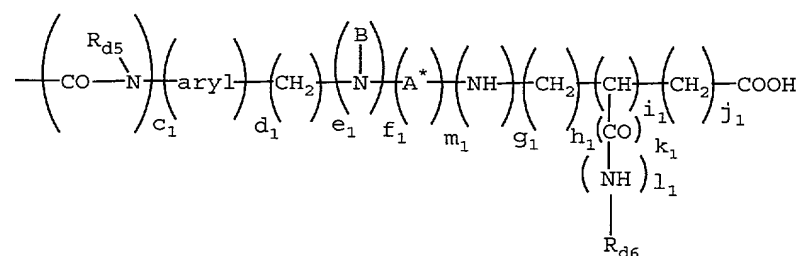
where

c and d are zero to 1 providing c and d are not simultaneously zero;

e is zero to 5; and

f is zero to 3; or

(3)



where

$c_1, d_1, f_1, g_1, k_1, l_1$ and m_1 are each independently zero or 1,

where c_1, f_1 and g_1 are not simultaneously zero, and

where m_1 is not zero when f_1 or g_1 is 1;

i_1 is zero or 1, where k_1 and l_1 are zero when i_1 is zero;

e_1 is zero to 3

h_1 is zero to 5;

j_1 is zero to 2; and

the sum of e_1, h_1 and j_1 is 2 to 7;

A is $-\text{O}-$, $-\text{S}-$, $-\text{CH}=\text{CH}-$, or $-\text{N}(\text{R}_{d6})-$;

R_{d2} and R_{d3} are independently H, alkyl, cycloalkyl or heteroaryl;

5

10

X is



15

the sum of h, i and j is > 1 and < 4 ;

k and m are independently zero or 1, with n being other than zero when m is 1; and

the sum of l, m and n is ≥ 2 and ≤ 5 ;

20



25

Q_{2e} is

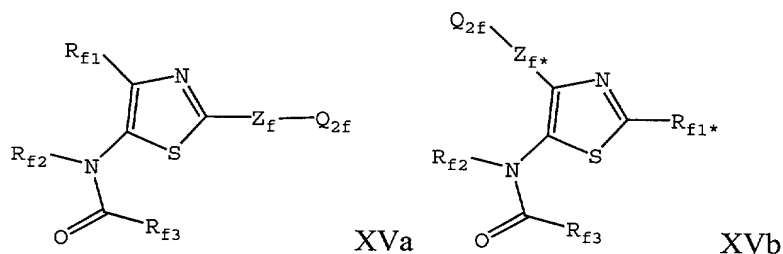
(2) aryl optionally substituted with one group selected from halo, hydroxy, alkoxy nitro, $-NH_2$, $-alkyl(NH_2)$, $-C(O)NH_2$, $-alkylC(O)NH_2$ or $-arylC(O)NH_2$; or

134

R_{e1} is H, alkyl, hydroxyalkyl, halogen or carboxy; and

R_{e2} is H, $-C(O)alkyl$, $-SO_2alkyl$ or $-C(O)phenyl$ optionally substituted with halogen;

(f) a compound of formula XVa or XVb



where

Z_f is $-CR_4R_5-$, $-O-CR_4R_5$, or $-NR_4-$; ;

Z_{f*} is $-CR_4R_5-$;

Q_{2f} is aryl or heteroaryl;

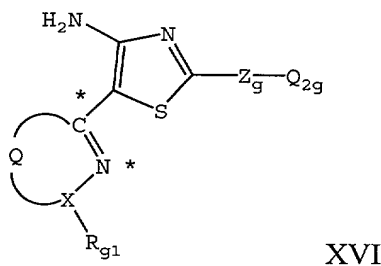
R_{f1} is alkyl, aryl, heteroaryl, or cycloalkyl;

R_{f1*} is H, alkyl, cycloalkyl, alkoxy, alkenyl, alkynyl, aryl, heterocyclo, amino-substituted alkoxy, nitro, hydroxy, or NH_2 ;

R_{f2} is H, alkyl, aryl, heteroaryl, or cycloalkyl; and

R_{f3} is H, alkyl, cycloalkyl, aryl, halo, CF_3 , or heterocyclo;

(g) a compound of formula XVI



where

Z_g is $-NH-$ or $-NH-CR_4R_5-$;

Q_{2g} is aryl, heteroaryl;

X is C or N

Q is a divalent radical containing 2 or 3 ring atoms each independently selected from C, N, O, S, CR_{g1} , NR_{g1} , which together with C^* and N^* form a 5 or 6-membered aromatic or nonaromatic ring;

R_{g1} is hydroxy, halo, cyano, nitro, alkyl, alkenyl, cycloalkyl, non-aromatic heterocyclo, aryl, heteroaryl, or $-C(O)R_{g2}$;

or R_{g1} cycloalkyl, heterocyclo or aryl that is fused to Q;

R_{g2} is H, alkyl, cycloalkyl, non-aromatic heterocyclo, aryl, heteroaryl or
 5 $-OC(O)R_{g3}$;

R_{g3} is H, alkyl, cycloalkyl, non-aromatic heterocyclo, aryl, heteroaryl or $-C(O)NR_{g4}R_{g5}$;

R_{g4} and R_{g5} are independently H, alkyl, cycloalkyl, heterocyclo, aryl or
 $-C(R_{g6})=NR_{g7}$;

10 R_{g6} is H, alkyl, cycloalkyl, heterocyclo, aryl, amino, alkylamino, dialkylamino or $-SO_2R_{g8}$;

R_{g7} is H, alkyl, cycloalkyl, heterocyclo, aryl heteroaryl, hydroxy, alkoxy, amino, alkylamino, dialkylamino, or $-C(O)$ amino;

R_{g8} is alkyl, cycloalkyl, heterocyclo, aryl or $-SO_2NR_{g9}R_{g10}$;

15 R_{g9} and R_{g10} are independently H, alkyl, cycloalkyl, heterocyclo, aryl, or $-OR_{g11}$;

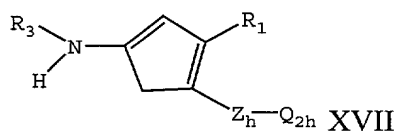
R_{g11} is alkyl, cycloalkyl, heterocyclo, aryl, $-C(O)R_{g2}$, $-OC(O)R_{g3}$, $-C(O)NR_{g4}R_{g5}$, $-NR_{g12}R_{g13}$, or $-SR_{g14}$;

R_{g12} is H, alkyl, cycloalkyl, heterocyclo, aryl, hydroxy, alkoxy, amino, $-C(O)R_{g2}$, $-OC(O)R_{g3}$, $-C(O)NR_{g4}R_{g5}$, or $-C(R_{g6})=NR_{g7}$;

20 R_{g13} is H, alkyl, cycloalkyl, heterocyclo, aryl, $-C(O)R_{g2}$, $-OC(O)R_{g3}$, $-C(O)NR_{g4}R_{g5}$, $-C(R_{g6})=NR_{g7}$, $-SO_2R_{g8}$, or $-SO_2NR_{g9}R_{g10}$; and

R_{g14} is H, alkyl, cycloalkyl, heterocyclo, aryl or $-C(O)NR_{g4}R_{g5}$; or

25 (h) a compound of formula XVII



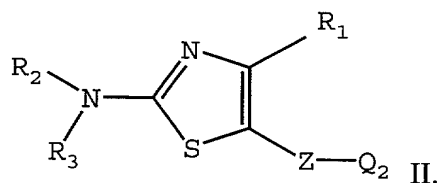
where

Z_h is $-S-$ or $-S(O)_q-CR_4R_5-$; and

Q_{2h} is heteroaryl

30

2. A compound of claim 1 having the following formula II



3. A compound of claim 1 wherein

Q₂ is optionally substituted phenyl;

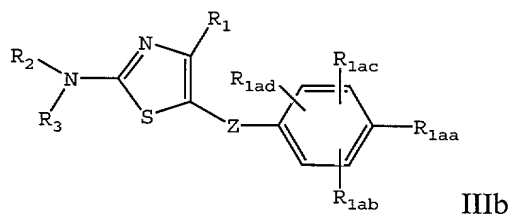
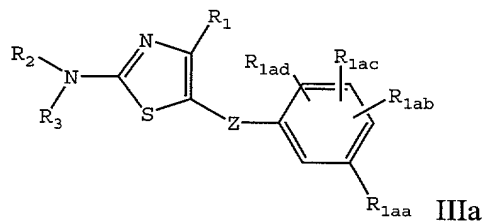
- 5 Z is selected from -S-, -CR₄R₅-S-, -S-CR₄R₅-, -CR₄R₅-O-CR_{4a}R_{5a}-,
 -CR₄R₅-NR_{4b}-CR_{4a}R_{5a}-, -CR₄R₅-, -CR₄R₅-SO₂- or -CR₄R₅-S(O)-;
 R₂ is hydrogen or alkyl; and
 R₃ is H, -Z₄R_{6a} or -Z₄NR_{7a}R_{8a}.

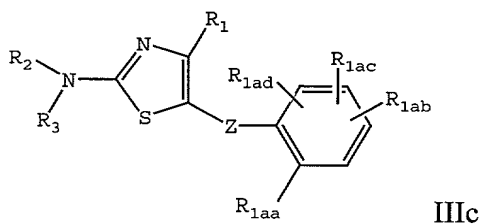
- 10 4. A compound of claim 3 wherein the Q₂ phenyl is independently
 substituted with alkyl, hydroxy, alkoxy, haloalkoxy, halo, nitro, -C(O)_qR₆, -C(O)_qH,
 -Z₄-NR₇R₈, -Z₄-N(R₁₂)-Z₅-Z₆, or -Z₄-N(R₉)-Z₅-NR₁₀R₁₁).

15 5. A compound of claim 4 wherein R₃ is -Z₄R_{6a}.

6. A compound of claim 5 wherein Z is -S-, -CR₄R₅-S-, or -S-CR₄R₅-.

7. A compound of formula IIIa, IIIb or IIIc





including diastereomers, enantiomers and salts thereof

where

Z is

- | | |
|----|--|
| 5 | (1) -O-, |
| | (2) -S-, |
| | (3) -CR ₄ R ₅ -O-CR _{4a} R _{5a} -, |
| | (4) -CR ₄ R ₅ -NR _{4b} -CR _{4a} R _{5a} -, |
| | (5) -CR ₄ R ₅ -S-CR _{4a} R _{5a} -, |
| 10 | (6) -CR ₄ R ₅ -O-, |
| | (7) -CR ₄ R ₅ -NR _{4b} -, |
| | (8) -CR ₄ R ₅ -S-, |
| | (9) -S-CR ₄ R ₅ -, |
| | (10) -S(O) _q -, |
| 15 | (11) -CR ₄ R ₅ -S(O) _q -, or |
| | (12) -S(O) _q -CR ₄ R ₅ -; |

R₁, R_{1ab}, R_{1ac} and R_{1ad} are independently

- | | |
|----|---|
| | (1) hydrogen or R ₆ , |
| | (2) -OH or -OR ₆ , |
| 20 | (3) -SH or -SR ₆ , |
| | (4) -C(O) _q H, -C(O) _q R ₆ , or -O-C(O) _q R ₆ , where q is 1 or 2, |
| | (5) -SO ₃ H or -S(O) _q R ₆ , |
| | (6) halo, |
| | (7) cyano, |
| 25 | (8) nitro, |
| | (9) -Z ₄ -NR ₇ R ₈ , |
| | (10) -Z ₄ -N(R ₉)-Z ₅ -NR ₁₀ R ₁₁ , |
| | (11) -Z ₄ -N(R ₁₂)-Z ₅ -R ₆ , or |
| | (12) -P(O)(OR ₆) ₂ ; |

R_{1aa} is $-C(O)_qH$, $-C(O)_qR_6$, $-Z_4-NR_7R_8$, $-Z_4-N(R_9)-Z_5-NR_{10}R_{11}$ or $-Z_4-N(R_9)-Z_5-R_6$;

R_2 and R_3 are each independently H, $-Z_4-R_{6a}$, or $-Z_4-NR_{7a}R_{8a}$;

R_4 , R_{4a} , R_5 and R_{5a} are each independently hydrogen, alkyl, aryl, aralkyl, cycloalkyl, or heteroarylalkyl;

- 5 R_6 , R_{6a} , R_{6b} and R_{6c} are independently alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, heterocyclo, or heterocycloalkyl, each of which is unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 ,

- 10 R_7 , R_{7a} , R_8 , R_{8a} , R_9 , R_{10} , R_{11} and R_{12}

(1) are each independently hydrogen, or $-Z_4R_{6b}$; or

(2) R_7 and R_8 , or R_{7a} and R_{8a} may together be alkylene, alkenylene, or heteroalkylene, completing a 3- to 8-membered saturated or unsaturated ring with the nitrogen atom to which they are attached, which ring is

- 15 unsubstituted or substituted with Z_1 , Z_2 and one or more groups Z_3 , or

(3) any two of R_9 , R_{10} and R_{11} may together be alkylene, alkenylene or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

- 20 Z_1 , Z_2 and Z_3 are each independently

(1) hydrogen or Z_6 ,

(2) $-OH$ or $-OZ_6$,

(3) $-SH$ or $-SZ_6$,

(4) $-C(O)_qH$, $-C(O)_qZ_6$, or $-O-C(O)_qZ_6$,

- 25 (5) $-SO_3H$, $-S(O)_qZ_6$, or $S(O)_qN(Z_9)Z_6$,

(6) halo,

(7) cyano,

(8) nitro,

(9) $-Z_4-NZ_7Z_8$,

- 30 (10) $-Z_4-N(Z_9)-Z_5-NZ_7Z_8$,

(11) $-Z_4-N(Z_{10})-Z_5-Z_6$,

(12) $-Z_4-N(Z_{10})-Z_5-H$,

- (13) oxo,
- (14) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be alkylene or alkenylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached; or
- 5 (15) any two of Z_1 , Z_2 , and Z_3 on a given substituent may together be $-O-(CH_2)_q-O-$;

Z_4 and Z_5 are each independently

- (1) a single bond,
- (2) $-Z_{11}-S(O)_q-Z_{12}-$,
- 10 (3) $-Z_{11}-C(O)-Z_{12}-$,
- (4) $-Z_{11}-C(S)-Z_{12}-$,
- (5) $-Z_{11}-O-Z_{12}-$,
- (6) $-Z_{11}-S-Z_{12}-$,
- (7) $-Z_{11}-O-C(O)-Z_{12}-$,
- 15 (8) $-Z_{11}-C(O)-O-Z_{12}-$; or
- (9) alkyl

Z_6 and Z_{6a} are independently

- (i) alkyl, hydroxyalkyl, alkoxyalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aralkyl, alkylaryl, cycloalkylaryl, heterocyclo, or heterocycloalkyl;
- 20 (ii) a group (i) which is itself substituted by one or more of the same or different groups (i); or
- (iii) a group (i) or (ii) which is independently substituted by one or more of the groups (2) to (15) of the definition of Z_1 ;

25 Z_7 , Z_8 , Z_9 and Z_{10}

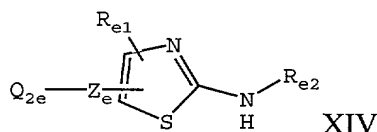
- (1) are each independently hydrogen or $-Z_4-Z_{6a}$;
- (2) Z_7 and Z_8 may together be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the atoms to which they are attached, which ring is unsubstituted or substituted with one or
- 30 more Z_1 , Z_2 and Z_3 , or
- (3) Z_7 or Z_8 , together with Z_9 , may be alkylene, alkenylene, or heteroalkylene completing a 3- to 8-membered saturated or unsaturated ring together with the

nitrogen atoms to which they are attached, which ring is unsubstituted or substituted with one or more Z_1 , Z_2 and Z_3 ;

Z_{11} and Z_{12} are each independently

- (1) a single bond,
- 5 (2) alkylene,
- (3) alkenylene, or
- (4) alkynylene;

provided said compound is other than a compound of formula XIV



10 where

Z_e -S-, -S(O)_q- or -CH₂-S(O)_q-;

Q_{2e} is phenyl optionally substituted with one group selected from halo, hydroxy, alkoxy nitro, -NH₂, -alkyl(NH₂), -C(O)NH₂, -alkylC(O)NH₂ or -arylC(O)NH₂;

15 R_{e1} is H, alkyl, hydroxyalkyl, halogen or carboxy; and

R_{e2} is H, -C(O)alkyl, -SO₂alkyl or -C(O)phenyl optionally substituted with halogen.

8. A compound of claim 7 having the formula IIIa.

9. A compound of claim 8 where

Z is -S-, -CR₄R₅-S-, or -S-CR₄R₅-;

R₂ is hydrogen or alkyl; and

R₃ is -Z₄R_{6a}, where:

25 (a) Z₄ is a single bond and R_{6a} is heteroaryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;

(b) Z₄ is -C(O)- and R_{6a} is

- (1) aryl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;
- (2) alkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ;
- 30 (3) cycloalkyl optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or
- (4) heterocyclo optionally substituted with one or more Z_1 , Z_2 or Z_3 ; or

- (c) Z_4 is $-\text{C}(\text{O})-\text{O}-$ and R_{6a} is alkyl, cycloalkyl, aryl or aralkyl, any of which may be optionally substituted with one or more Z_1, Z_2 or Z_3 .

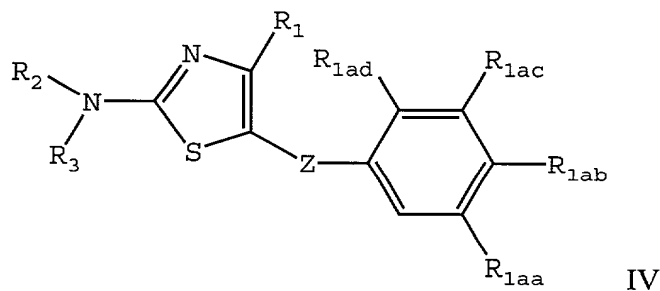
10. A compound of claim 9 wherein

5 R_{1aa} is $-\text{C}(\text{O})\text{R}_{6a}$ or $-\text{Z}_4-\text{NR}_7\text{R}_8$; and

$\text{R}_{1ab}, \text{R}_{1ac}$ and R_{1ad} are independently H, alkyl, hydroxy, nitro, halo, $-\text{OR}_6$, $-\text{NR}_7\text{R}_8$, $-\text{C}(\text{O})_q\text{H}$ or $-\text{C}(\text{O})_q\text{R}_6$.

11. A compound of claim 10 wherein at least one of $\text{R}_{1ab}, \text{R}_{1ac}$ and R_{1ad} is other than H.

12. A compound of claim 8 having the following formula IV



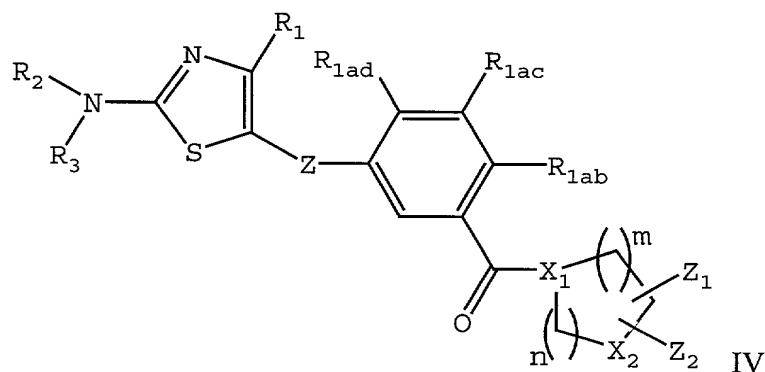
where one of $\text{R}_{1ab}, \text{R}_{1ac}$ and R_{1ad} is H and the other two are independently alkyl, hydroxy, nitro, halo, $-\text{OR}_6$, $-\text{NR}_7\text{R}_8$, $-\text{C}(\text{O})_q\text{H}$, or $-\text{C}(\text{O})_q\text{R}_6$.

13. A compound of claim 12 wherein one of $\text{R}_{1ab}, \text{R}_{1ac}$ and R_{1ad} is H and the other two are independently alkyl or $-\text{OR}_6$.

14. A compound of claim 13 wherein Z is $-\text{S}-$ and R_{1c} is H.

15. A compound of claim 13 wherein Z is $-\text{S}-\text{CR}_4\text{R}_5-$, and R_{1d} is H.

16. A compound of claim 12 having the following formula V



where

X_1 is C or N;

X_2 is CZ_{3a} , NZ_{3a} , O or S;

- 5 Z_{3a} is H, hydroxy, optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted aryl, optionally substituted aralkyl, $-OZ_6$, $-C(O)_qH$, $-C(O)_qZ_{6a}$, $-Z_4-NZ_7Z_8$, or $-Z_4-N(Z_{10})-Z_5-Z_6$;

n is 1 to 3; and

m is zero to 2.

10

17. A pharmaceutical composition comprising at least one compound of claim 1 and a pharmaceutically acceptable vehicle or carrier therefor.

- 15 18. A pharmaceutical composition of claim 17 further comprising at least one additional therapeutic agent selected from anti-inflammatory agents, anti-proliferative agents, anti-cancer agents or anti-cytotoxic agents.

- 20 19. A pharmaceutical composition of claim 18 wherein the additional therapeutic agents are selected from steroids, mycophenolate mofetil, LTD_4 inhibitors, CTLA4-Ig, LEA-29Y, phosphodiesterase inhibitors, antihistamines, or p^{38} MAPK inhibitors.

- 25 20. A method of treating a Tec family tyrosine kinase-associated disorder comprising the step of administering to a patient in need thereof, an effective amount of at least one compound of claim 1.

21. The method of claim 20 wherein the Tec family tyrosine kinase-associated disorder is an Emt-associated disorder.

- 5 22. The method of claim 21 wherein the Emt-associated disorder is selected from transplant rejection, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, lupus, graft vs. host disease, T-cell mediated hypersensitivity disease, psoriasis, Hashimoto's thyroiditis, Guillain-Barre syndrome, cancer, contact dermatitis, allergic disease, asthma, ischemic or reperfusion injury, atopic dermatitis, allergic rhinitis, or chronic obstructive pulmonary disease.